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The Cerebrospinal fluid and its routine examination

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AND

ITS ROUTINE EXAMINATION

by

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INTRODUCTION

Since the establishment of the spinal puncture, experimemters have investigated the cerebrospinal fluid, its physiological properties and its pathological reactions by every means at their disposal. Through the analysis and study of thousands of fluids representing every imaginable type of disease process, clinical pictures have been identified with fluid syndromes. In the course of there investigations it was found that pathological conditions could be recognized by knowledge of only certain properties and contents of the fluid. During the present age physicians use only a few simpler tests in their clinical fluid studies. It is the purpose of the paper to consider these routine tests, their rationale' and signifigance.

C.B.

HISTORY

In the subarachnoid space surrounding the brain, there exists a clear, colorless fluid of a slight but definite viscosity. This is the cerebrospinal fluid. Since the creation of mankind, this fluid has existed, functioned and undergone changes--both pathological and physiological--and yet, it is a comparatively recent discovery.

The ancients were entirely unaware of its identity as a specific secretion. The learned Greeks knew of its presence only in cases of hydrocephalus. They are thought to have tapped the brain in such cases, but they considered it as merely another of man's many pathological manifestations. (82)

Hippocrates considered the brain a gland which produced the fluid poured into the pharynx through the ethmoid bone. This mucous discharge was named after the pituitary gland. He did not know of the fluid proper.(82)

Herophilus (300 B.C.) described the ventricles and the choroid plexus, but did not know of their function. It is possible that this observation is contained in one of his lost books. He was interested particularly in finding a seat for the soul--the search for which has probably delayed scientific progress as greatly as the dark ages. Erasistratus of Julius (330 B.C.) also described the four cavities of the brain but did not mention any such fluid. Galen did not mention the

fluid as we know it today, although he is quoted as writing about "an excrementitial liquid expressed from several places in the brain into the ventricles, especially the fourth, where this liquid is stored and then purged into the nose through the ethmoid bone and infundibulum."(55)

In 340 A.D., following a lapse of several centuries we find the record of Hemesius of Emerea. He also described the ventricles which he believed contained the mental powers. Vesalius wrote pages in description of the choroid plexus and ventricles, but also made no mention of the fluid.(16)

Leonardo da Vinci in 1452 noticed the ventricles and wrote pages and drew many sketches of what he thought were their relationships, but he does not describe the fluid.(55)

The first record of the cerebrospinal fluid is found in the works of Varoli (1543-1575). He insisted that the cavities of the brain were filled, not with pneuma as was the popular conception, but with a fluid. Little credit has been given him because he failed to describe the fluid which he claimed present, although he did believe that the ventricles served as pumps for this fluid. (16)

Glissen (1597-1677) did notice the fluid but it evidently did not arose any questions in his mind. (16)

Willis in 1669 studied the ventricles but did not notice the fluid, or if so attached no signifigance to them. (16)

Vieussens and Sylvius (1700) found fluid which they ascribed to the "pituitary, pineal and choroid glands." (10) Vieussens thought it a vehicle for the animal spirits contributed by the blood. He also believed that this fluid was barred from the subtentorial region, becuse of a valve which now bears his name. (19)

Weil in 1727 noticed a clear fluid flowing from the ear following a head injury, but did not attempt to learn the source. (16)

The actual discovery of the fluid is credited to one Dominico Contugno. In 1764 he demonstrated its presence in fishes and amphibians. He was unable to show it in dogs and humans, probably because in the lower animals this exists as a jelly rather than a liquid. Bilanchoni claims that Valsalve wrote a few years earlier of "an ounce of a certain fluid in cutting the cord membrane of a dog, the fluid resembling that seen in articulations." (54)

Sommering followed these investigations with other work. However, he advanced the knowledge of this fluid very little because of religious motives. He considered

the fluid as the true "organ of the soul." (82) Somewhat later in the same year Robert Whytt wrote a book on the acute brain diseases. These he discussed under the general heading "Dropsies of the Brain" with particular attention to tubercular meningitis. (16)

Not until 1766 was there an adequate description of the fluid. In the third Latin edition of his Physiology Albertus von Haller considered the fluid as being of the same type as that found in the "pericardium, pleura, tunica vaginalis, amnios, joints, renal capsules, and probably womb, with juices of the stomach and intestine, and lastly the lymph generally known." (55) Haller also considered the problem of drainage of this fluid. "Have lymphatic vessels been seen in the brain? They have been described in the large choroidal plexus amongst the fibers of the olfactory nerve, and in the pia mater. For my own part, I have never seen them, and it is probable that there are none, since there are no conglomerate glands in the brain, which are always found near these vessels. As for the various accounts which are give of the pituitary glands, of the infundibulum and of the ducts which lead from thence into the veins of the head, absorbing water from the ventricles, they are not supported by any anatomic demonstration; which makes it probable that the vapor,

which is secreted into the ventricles of a healthy person, is in like proportion, absorbed again by the inhaling veins; and that if there be any excess, it descends through the bottom of the ventricles to the basis of the skull, and into the loose cavity of the spinal marrow. That this is the case, appears from the palsies, which ensue after apoplexies and from the watery tumors in the lower part of the spinal marrow, in hydrocephalic patients." (55) Haller believed that the liquid was not only secreted from the medullary tubes, but was contained by them and the tubes around the nerves. Despite his knowledge of the cerebrospinal fluid, he had no conception of its true function. (16) He believed the fluid to be the instrument of sense and motion, and to consist of elastic and electrical matter. (82)

There was no attempt to explain the presence of the fluid until Magendie published his papers in 1825. Here we also find the first complete description of the cerebrospinal fluid. "The canal which is formed around the medulla by the pia mater, and which is lined by the arachnoid, is a great deal larger than necessary to contain the organ: but during life the whole internal is filled up by a serous fluid which spouts out to many inches in height from a small

puncture made in the dura mater. An analogous arrangement is also to be observed around the brain and cerebellum. I have given to this fluid the name cephalorachidian, or cephalospinal." He concieved that this fluid was protective in function because it encased the entire brain in a "water jacket" and also that it "surrounded by a very fine serous membrane the principal use of which is to yield a thin fluid which lubricated the brain." (54)

The men immediately following Magendie studied the fluid from various angles. There were Luschka and Ecklar who looked at the problem from the anatomical point of view. Cavazzani considered the physiologic side, while Nauyn dealt with the physical aspects. In 1842 Lange's "Anatomy" gave much space to an exclusive discussion of the cerebrospinal fluid. (54)

Only after Lange did the workers consider the source and nature of the fluid. In 1850 Carl Schmidt expressed the opinion that the cerebrospinal fluid was more than a mere transudate. Faivre (1853) regarded it as a secretion. These two view points still persist and it is interesting to note that despite the number of experiments that have been and are being carried out for the purpose of determining this one fact, very little has been definitely proven. (51)

In later years the more rapid advancement in the study of the cerebrospinal fluid is due in a large extent to the development of a means of removing the fluid from the living body. Originally the fluid was removed from the skull. This envolved a scalp wound, trephining of the skull, a great number of instruments, experience, and a great risk to the patient. It is remarkable that as much could be learned from such a complicted and dangerous technique. (9)

Credit for the first spinal puncture is given to Corning. In 1885 he introduced a needle into the intravertebral cavity for the purpose of cocainizing the cord in certain spinal affections. He entered at a lower dorsal level, which introduced a large element of risk into the proceedure. However, he left no trace on record of his instruments and technique. (16)

Essix Wynter (1891) drained the fluid in cases of tubercular meningitis. He drained the fluid continuously by means of a trocar and cannula. All patients showed immediate improvement, but subsequently died of the disease. Later in the same year Morton used his technique with similar results. (55)

This method of puncture was improved by Quincke (1891). The method of Corning was too dangerous, that of Wynter involved the use of a large trocar and

continuous drainage. Quincke used a simple technique which has been improved very little in years past. He used a plain, strong needle inserted in a lower lumbar segment. Quincke reduced several cases of hydrocephalus by the use of this method and therefore concluded that puncture had a therapeutic value in the reduction of increased intracranial pressure. It was in 1893 that Lichtheim suggested its use as a diagnostic aid. Two years later there were many cases of puncture reported in various countries. Since 1896 the spinal puncture has been adopted as a proceedure fitted for both therapeutic and diagnostic purposes. (16)

From that time on there has been hardly a modern science that has not been concerned with the growth of our knowledge of this fluid. Chemistry, bacteriology, serology, and physiology have all played an important part in the development of the uses and knowledge of this fluid.

ANATOMY

The brain and cord are incased in a bony cage which protects them from the outside world. This cage is lined with a tough, fibrous membrane--one of three which surround the brain and cord--which is adherent to the bones of the cranial cavity and spinal canal (except from the first lumbar to the second sacral vertebrae). There is, however, a potential space between the two. This membrane, the dura mater, is in contact with a loose areolar membrane, the arachnoid. The membrane immediately covering the brain and dipping into all of its convolutions, thepia mater, is separated from the arachnoid membrane by the subarachnoid space. This space is not continuous, but in places there are small adhesions between the two which separate the space into small rectangular areas and thus prevent the free flow of the fluid. This subarachnoid space is the extraneural container for the cerebrospinal fluid. The subarachnoid space is normally a closed sac and fluid can not pass from it into the subdural space. This space differs in depth at the various levels. It is thin over the convexity of the brain, but bridges over the irregularities in contour to form lacunae and cisterns of fluid. The main one of these cisterns lies under the inferior surface of the cerebellum

and behind and at the sides of the medulla. This is the cisterna magna. It varies from three-quarters to an inch in depth over the foramen of Magendie. Another of the cisterns is the cisterna basalis which lies between the anterior-superior surface of the pons and optic chiasma is also fairly deep. In the spinal portion this space varies from one to several millimeters in depth except for the inferior portion. From the first lumbar to the first sacral vertebrae it may measure as much as one centimeter in depth and width. The spinal subarachnoid space is divided by the ligamentum denticulatum which passes from the pia at the sides of the cord to the dura mater where it attaches. There are prolongations of the subarachnoid space along the cranial and spinal nerves. These spaces are particularly noticeable along the optic, trigeminal, auditory and vestibular nerves. In the spinal subarachnoid space it is the posterior roots that have the most marked "perineural spaces."

The cerebrospinal fluid seems to arise from the choroid plexuses in the lateral, the third and the fourth ventricle. These are highly vascular fringes of invaginated pia mater which are covered with a layer of cuboidal cells on their ventricular surface.

These cells are continuous with and probably are derived from the ependyma of the ventricles. These cells are often clear, swollen and contain no definite nuclei.

The choroid plexus of the third and lateral ventricles resembles the letter W in shape. From the posterior part of the third ventricle where they are in contact the two halves of the plexus run forward to the foramen of Monroe. They pass through and separate, each going to the lateral ventricle on its respected side. They turn backwards, downwards and then forwards around the inner wall of the inferior horn of the lateral ventricle. There is no plexus in the anterior nor posterior horns of the lateral ventricle.

The plexus of the fourth ventricle is invaginated along two vertical lines close to the median plane and along two horizontal lines, which diverge from the vertical ones and run at right angles toward the lateral recess. These right and left halves are joined at the angle so that they resemble a T with a double verticle limb.

The choroid plexuses are merely vascular invaginations into the ventricles. They must, however, to function properly have a very good blood supply. The plexus in the inferior horn of the lateral ventricle is supplied by the anterior choroidal artery. This

arises from the main trunk of the internal carotid, passes into the choroidal fissure above the fimbria and joins the plexus in the inferior horn. The posterior choroidal artery is a branch of the posterior cerebral. It enters under the splenium of the corpus callosum to join the posterior end of the plexus in the third ventricle. It also supplies the plexus of the fourth ventricle.

The ventricles are so constructed that they form a compartment which is waterproof except for the opening into the subarachnoid space. When the plexus is torn from its attachment to the wall of the ventricle a large fissure which communicates with the ventricle is found. These fissures are filled with pia mater during life and, although thin, the pia maintains the isolation of the ventricle.

As we have mentioned previously the lateral and third ventricles are connected by the small channel, the foramen of Monroe. The third is connected by a narrow opening, the Aqueduct of Sylvius, with the fourth ventricle. The fourth ventricle opens into the subarachnoid space through a central foramen at the tip of the calamus scriptorus, the foramen of Magendie, and two lateral openings, the foramina of Luschka, at the tip of the lateral recesses.

There are certain prolongations of the sub-arachnoid space and of the ependyma of the ventricles along the vascular beds of the central nervous system. These are the Virchow-Robin or perivascular spaces. They are very minute and contain serous and waste materials. They have been called the lymphatics of the brain.

(41, 55, 61, 9.)

PHYSIOLOGY

SOURCE

Only after the development of the spinal puncture did the source of the fluid become a truly active question. Faivre in 1853 first described the glandular structure of the choroid plexus. His observations supported by Luschka's a short time later caused the abondonment of the earlier theory that the fluid was elaborated by the leptomeninges. (48)

The earlier investigators had to depend on the mere gross appearances and microscopic structure. They were aided particularly by clinical cases of hydrocephalus--especially those cases of internal hydrocephalus due to blockage of the cerebral aqueduct. Halliburton in 1889 described the fluid in detail but would not attempt to deal with "certain interesting questions such as source and final end of the fluid." (43)

His and Kolliker were the first to demonstrate the development of the meninges from the mesenchyma and the differentiation of cerebrospinal membrane to form the subarachnoid space. Other investigators showed that only after the development of the plexus did the cerebrospinal fluid appear. Weed has studied the relationships more fully in the embyoe and has reached the same conclusions. (48)(88)

There were only two sources probable for the source of the fluid passed into the ventricles. These were

the ependyma cells and the choroid plexus. (9) In 1902 Petit and Gerard found that certain drugs such as pilocarpine and muscarine seemed to increase the formation of the fluid. On examination these cells which had been submitted to the action of such a drug showed many droplets of liquid. They considered this evidence that the cerebrospinal fluid was secreted by the choroid plexus. Mott considered the source of the fluid the same and gave the choroid plexus the name "choroid gland." He compared it to the lacrimal gland which he thought it resembled. (16)

Cushing did other experimental work in observing cases where the proencephalic cavity communicated with the ventricles. By the use of ether (an activator similar to those drugs previously mentioned) as anesthetic he was able to see droplets of liquid exuded from the plexuses. (48)

In 1919 Dandy proved the source of the fluid quite substantially. In the words of one author, "Dandy's experiment furnishes the strongest single substantiation of the hypothesis that the choroid plexuses elaborate the cerebrospinal fluid." (9) Dandy removed the choroid plexus on the one side of the brain and blocked the aqueduct of Sylvius. On the other side he did not remove the plexus.

The side on which the choroid plexus was removed did not change while the other side developed an internal hydrocephalus.(9)

However, this does not prove this is the only source of the fluid. In fact, such is not the case. One of the most notable indications of a second source is the fact that the ventricular and spinal fluids differ. Dandy and Blackfan (1914) found that in cases of internal hydrocephalus with complete block of the aqueduct they could remove only a small amount of fluid at a time, but that in a short period a similar amount could be withdrawn. (9)

If there is a second source of the fluid it must be either directly through the arachnoid coat or from the perivascular elongations. Earlier investigators had decided that the meninges had nothing to do with the origin of the fluid. Their surmises had been substantiated by the work of Dandy.

In 1900 Spina increased the pressure of the fluid and on exposure noted that there was an exudation of clear points of liquid issuing from the surfaces of the ventricles. He argued that the flow of the fluid was towards and not away from the subarachnoid space. (9)

Weed surrmounted the difficulty of separating the two sources of the fluid by the introduction of a

cannula into the aqueduct of Sylvius. (88,48) His technique has been valuable not only in the finding of a second source but also in proving the mechanism of absorption of the fluid. He first made an injection of potassium ferrocyanide into the subarachnoid space, then hardened the brain in situ with a little formalin and one per cent hydrochloric acid. In sections of the tissue he found that the Prussian blue granules go to the end of the perivascular spaces but do not pass on into the blood vessels. Therefore he concluded that the flow of the fluid takes place away from the vessels into the subarachnoid space and not the reverse as had been Mott's opinion. (88,9,64)

Cushing (1914) also furnished further proof of this source of the cerebrospinal fluid. He pointed out that, in cases of high pressure where the exit of the perivascular spaces was obstructed by the pressure of its convolutions against the surface, the spaces are distended to a teriffic extent. This explains not only a second source for the fluid but suggests a possible function for the fluid. Probable that the fluid from these spaces carries out the products of neural metabolism. This is indicated by the presence of waste materials in the fluid and the close relationship between the perivascular and peineural channels. (16,9)

Katzenelbogen (1935) after a comprehensive review of the literature concludes that the main source of the fluid is in the choroid plexus, that there is no evidence for the ependymal production of the fluid, that the studies on vital coloration demonstrate that the plexuses are the main pathway from the general circulation to the cerebrospinal fluid but do not justify the claim that the choroid plexuses produce the fluid, and that the difference in the composition of the ventricular and subarachnoid fluid inicates an extraventricular source. (51)

More study indicates that there may be additions to the fluid from the various parts of the brain. Evidence seems to show that the secretion of the pituitary is emptied into the fluid. Cushing and Goetsch and Boyd have also noticed properties of the fluid which would indicate this fact. These observations have opened an entirely new field to the experimenter.(9)

MECHANISM

One of the pertinent problems confronting the investigators was the mechanism of production of the fluid. The earliest theory evolved for solving this problem was that the fluid was a transudate. Jolly (1871) believed that the "cerebrospinal fluid is a blood transudate and it is beyond doubt partly a result of

transudation from surrounding blood vessels, and partly from lymph spaces surrounding the blood vessels in the brain. (55) As noted previously, as early as 1850 Carl Schmidt had expressed the opinion that the fluid was more than a transudate. The facts do not bear out this theory. First, it does not resemble any of the other boly transudates, most important of which is lymph. It contains only .018 per cent albumin in contrast to blood albumin of 6.5 per cent (4.5 per cent of which appears in the lymph). Polanyi considered the low protein content as evidence that the fluid was not a transudate, for the filtration through the capillaries is a course one and even large molecules of albumin are enabled to pass. Leopold and Bernard consider that the lack of uric acid is evidence against the secretion theory. (54)

Another of the theories for the mechanism of production is the secretion of the fluid by the plexus. Willis in 1664 noticed a granular appearance in the cells of the plexus. (16) Cavazzani (1893) thought that the alkalinity of the fluid was less than that of blood. (54) Valentin (1836) described droplets of fat-like substance in the plexus epithilium which, he believed, were liable to turn into pigments. (51) In 1855 Luschka noticed there were clear cells without nuclei

which grew in size, approached the surface and finally discharged into the cavities. (51) Findlay (1889) noticed that "Where there are several layers of cells in situ, it may be made out that this vaculation increases steadily as we pass to the free surface, until cells are reached entirely transformed into globules showing no nuclear staining. Beyond these, again, the cells discharge their contents by breaking up, sometimes leaving an empty cell membrane to indicate where they have been." (51) Galeotti (1897) noticed globules in the cells and hollows on the external surface of others which he thought were once the site of globules. (16) Cavazzani in 1899 noticed that lymphagogues increased the flow of the fluid but did not influence the amount of ash. (16) In 1900 Cappelletti noticed that pilocarpine and ether increased the flow. He also thought that there was a decrease in the alkalinity. (54) Petit and Gerard (1902) saw the formation and expulsion of globules. (16) Mott (1910) believed that its composition proved it a secretion. He noticed the low protein already mentioned and also the fact that there were no lipochrome, leucocytes, agglutinins, haemolase, or alexins in the fluid. (16)

Perhaps we can summarize the findings in this somewhat satirical conclusion of Levinson. "From the

data presented, one would be inclined to believe that the choroid plexus is located in the ventricle for some purpose--possibly for the secretion of the cerebrospinal fluid. Yet the evidence brought forward to prove this point is not altogether convincing. (54)

However, is this a case of secretion such as that in milk, sweat, bile, and saliva? In these cases there is something specific added to the secretion, something the result of the vital activity of the cells engaged in the process. Here we have no substance added but rather certain substances withheld. (54) Against the theory of secretion is quite an array of evidence. Petit and Gerared later showed that these changes they had observed in the cells were due to post mortem changes and were not secretory activity. (51) Meek in 1907 observed that when stimulated the cells of the plexus became swollen which is different from other secretory cells which grow smaller when functioning. He also noted that the outer zone became clear while the inner zone was granular--the reverse of true excretory cells. (16) Other facts against the secretory theory are that the pressure of the fluid is lower than that of the intracranial capill ries, that under normal conditions there are no substances present which are not in the blood stream, colloids are entirely lacking, and there is an

increase in the urea content and glucose content of the fluid when there is a rise in their levels in the blood stream. (41) In 1921 Becht and Gunnar noticed that the fluid forced out by the action of pilocarpine returned to the ventricles when the pressure of the arteries decreased. (16)

Thus we have the secretory theory based on the histological and pharmacodynamic characteristics of the plexus. However, some observers say that the histological changes are due to post mortem conditions, that the action of certain drugs is due to the increase in blood pressure and also that there is nothing new added to the fluid which is not in blood. (51)

In 1912 Mestrezat stated that the fluid was not a filtrate, transudate or a secretion but a dialysate. (54) He believed that it was a case of selective filtration. (9) He believes that the fact that the pressure of the fluid may be increased without a rise in blood pressure would be too difficult a task for a simple restrainer. He noticed that certain substances foreign to the blood would not pass through the capillary endothelium even when they are of small molecule. He believed that the selective filtration was a characteristic shared by the capillaries of the brain, cord, and meninges and accounted for the increased permiability in meningitis. (41)

Bard (1917) estimated that the area of the choroid cells were about one meter. He stated that this was large enough so that cells of the plexuses merely played the part of a dialysing membrane. (16) It was in 1921 that Mestrezat and Ledebet were able to dialyze horse serum through a collodion membrane and obtain a result very similar to spinal fluid in composition. (16)

Fremont-Smith (1927) concluded that as a whole the evidence was overwhelmingly in favor of dialysis. He also thought that the simple laws governing this membrane equilibrium had a fundemental signifigance in the mechanism of fluid exchange in the body. (29) Flexner (1934) believes that evidence "which is far from ideal" suggests that the fluid is not a dialysate in equilibrium with the blood plasma or an ultrafiltrate, for the pressure in the capillaries of choroid plexus is too small to account for the free energy change which takes place in the generation of the fluid, but a secretion in the sense that cells must do work in its formation. (27) Walker (1933) states that the ciliary epithelium and the choroidal epithelium exhibit selective qualities not possessed by capillary endothelium or by the glomerular membrane, ane that neither the cerebrospinal fluid nor the humor is formed by simple process of

filtration or dialysis. (85) Katzenelbogen (1935) concludes that since we can not call it transudation or secretion or dialysis, we should call it "physiologic or biologic permiability" and that way also explain the spontaneous changes in the function of the barrier.(51)

ABSORPTION

The absorption of the fluid has been a problem which has bothered the experimenters in this field for many years. We have mentioned above that the fluid is secreted constantly and therefore must be just absorbed just as continually. It has been estimated that the fluid may be replaced from four to five times daily. (41) Since the total quantity of fluid in the entire subarachnoid space is somewhere about 120 ccm. it is evident that a very rapid and extensive absorption must take place. In cases of fractured base of the skull large quantities have been collected, as much as from one to two liters in the course of twenty-four hours. (9) Such demonstrations have incited much debate and experimentation as to the normal means of absorption.

Leonard Hill (1896) found that when saline colored with methylene blue was injected into the subarachnoid space the dye appeared in the bladder and stomach in from ten to twenty minutes, while the lymphatics showed no trace of the color in a much longer time. (at least

one hour). (41) Lewandowsky at about the same time used similar technique but with potassium ferrocyanide and regained the drug from the urine in twenty minutes. Although these proved that the cerebrospinal fluid is absorbed by the blood stream, the question of the mechanism involved still remained. (9)

At first the fluid was thought to be absorbed through the Pacchionean granulations. Key and Retzius injected gelatine under pressure and found the gelatine later in the spaces, the granulations and the sinusoids. (16) There were even trace of the gelatine in the lymphatics, but examination showed they had been ruptured, and thus, no conclusions could be drawn. (41) In 1900 Quincke injected into live animals a suspension of cinnabar granules. He later killed the animals at various intervals. He demonstrated the granules of cinnabar in the arachnoid granulations, sinuses, and even in the cervical lymph nodes. (48)

Later, many observers could not find the Pacchionian granulations in children and lower animals and concluded that they were merely pathological manifestations. (41) This led to the formation of many erroneous theories. Cushing believed that it might be through valves between the space and the veins. Mott thought that it was along the perivascular spaces and into the capillaries. Dandy and Blackfan (1914) felt that it was a diffuse process

from the entire subarachnoid space and that the cerebral portion was more efficient than the spinal. (9)

Later, the anatomists demonstrated that although there were not Pacchionian granulations present in all individuals there was a number of small villous projections into the venous sinuses of the skull. Then the theory of Key and Retzius was revived by Weed. In the years of 1914-1923 Weed did more work to prove the mechanism of absorption than any other man. He hardened the brain in situ in formalin with one per cent hydrochloric acid and was able to trace the granules resulting from a preliminary antemortem aubarachnoid injection of potassium ferrocyanide and iron ammonium citrate into the minutest ramifications of the space. He found most of the granules localized in the subarachnoid space, the nervous tissue being entirely free from color. Most of the granules could be traced directly into the villi, especially those in the cavernous sinus. The sinuses also contained some granules and it was possible to find granules actually passing through the mesothelial cells. He removed an amount of the fluid equal to that which he was injecting. This made it possible to inject considerable amounts into the space without increasing the pressure beyond normal. He found no evidence of any passage between the cells nor

was there any migration of the granules into the capillaries. Weed also injected carbon particles into the subarachnoid space and found that these do not pass into the sinuses of the skull. Thus he concluded that the villi were not valves but rather were covered by a continuous membrane which acted as a filter. He believed that the dural covering of the villi was thin and fenestrated so that the villi were continuously bathed by venous blood. He also noticed that the villi seemed to be plugged by the large particals of carbon and that by the injection of a sufficient quantity he could produce a hydrocephalus. This suggested that the villi were the main source of absorption. (88,89,9,55)

Although the drainage through the villi was thought to be the main one, it could hardly be the only one. Weed and others had noted that there were no villi within the spinal subarachnoid space. This led to a search for another means of absorption of the fluid. There is a considerable definite extension of the subarachnoid space in the form of tubular sheaths which accompany many of the cranial and spinal nerves. These end in a cul-de-sac beyond which carbon granules do not pass. However, with the use of potassium ferrocyanide the lymphatics of the region are found deeply stained. Leonard Hill demonstrated this as

early as 1891 but he noted that it took much longer than the appearance of the dye in the blood stream. Weed has shown that the ferrocyanide passed from the perineural space into the lymphatics by way of a reticular network. This is best illustrated in the olfactory nerve where the channels are demonstrated more easily and are better defined. This accessory path is especially important because it is the only means by which the fluid may be absorbed from the spinal subarachnoid space. (54,88)

The possibility of the choroid plexus and ventricular absorption of the fluid is best answered in a review of the subject by Katzenelbogen. He concludes that under normal conditions the plexuses do not take a signifigant part in the process of ventricular absorption which, normally is extremely low. The capacity of the ventricular ependyma to resorb the cerebrospinal fluid under physiologic conditions is insignifigant if not entirely lacking. (51)

Perhaps the drainage of the fluid is best expressed in the words of Weed himself. "It seems fair to assume the absorption of the cerebrospinal fluid is a two fold process, being chiefly a rapid drainage into the great dural sinuses, and ina small part, a slow indirect escape into the true lymphatic channels." (88)

CIRCULATION

To the earlier investigators the cerebrospinal fluid was merely a more or less stagnant lake. A circulation of the fluid was hinted by Magendie and Key and Retzius. Cathelin (1903) claims that he was the first to apply the term "circulu" to movement of the cerebrospinal fluid within and its exit from the cerebrospinal cavity. (51) With the discovery of the continual production of the fluid, however, it was evident that the fluid must have at least a partial circulation. The fluid is for the greater part originated in the choroid plexuses. It arises partially in the third ventrical from which it passes by means of the foramen of Monro into the third ventricle. With additions from this ventricle it passes into the fourth by way of the aqueduct of Sylvius. It then reaches the subarachnoid space by the means of three openings (the foramina of Luschka and Magendie). It was thought at one time that these foramina did not exist as openings but were covered by an intact membrane. (41) It is accepted at present that these foramen do normally exist as such and are not formed by the dissector. (51)

The fluid pours from these openings into the large cisterna in the floor of the skull and then seeps slowly out into the main subarachnoid space. The fluid moves slowly due to many small septa from the arachnoid to the

pia mater which divide the space into many rectangular spaces and delay the flow of the fluid.

The circulation of the fluid may be divided into two main groups. That of the fluid of the ventricles which passes into the subarachnoid space and that portion of the fluid above the tentorium. Goldmann upon injecting Trypan blue into the lumbar subarachnoid space found that the greater part of the nervous system was stained with the dye but that the cerebral cortex remained unstained. Golla with a much improved technique has been unable to abtain more than a slight staining reaction in this area. (9) Fluids injected into the top of the subarachnoid space above the tentorium reach all parts of the nervous system. These and other experiments seem to prove that substances pass with comparative ease from the spinal sac into the lower cranial chamber, but that the flow of the fluid in the upper chamber is chiefly from above downwards. (9) It is probable that the small amount of fluid in the upper chamber, which is very thin, is formed from the perivascular spaces. This would count for the lack of or slight staining. Since the greatest absorption of the fluid is in the sinuses, especially the confuent sinus, the fluid would not need to pass from the lower chamber upward.

The fluid then passes to the sites of absorption

which we have shown are the arachnoid villi and the lymphatics to a lesser degree. The contact with the blood stream is direct and rapid. That drainage of fluid by way of the lymphatics is much slower due to its indirectness. The fluid must first traverse the perineural spaces, then a reticular network and finally the lymphatic system before it reaches the general circulation. The majority of the fluid passes from the subarachnoid space through the villi not only because of their rapidity, but also because of the greater filtration area in contact with the fluid. (41). For this reason the absorption from the cranial portion is much more rapid and conspicuous than from the spinal sac. (51)

The factors influencing the flow of the fluid are many. Those with the greatest action are stimulation of the choroid plexus and venous pressure. (9)

Dixon and Halliburton were able to destinguish rises of pressure due to true increased secretion from those rises of vascular origin. They found that certain substances act as true lymphagogues, those with a truly specific action being extracts of the choroid plexus and of brain. Normal fluid had no effect when injected, while that from cases of general paralysis and cerebral disintegration were followed by an increased flow. This suggested a hormone produced by the brain substance which

which stimulated the epithelial cells. (23) It has also been shown that the flow of the fluid is increased by the presence of excess carbon dioxide in the blood. A fact that has strengthened the metabolic viewpoint of the function of the fluid. Of great value in the study of the cerebrospinal fluid is the fact that those substances which increase the rate of production also increase the pressure--thus the high pressure in the cases of general paralysis and cerebral disintegration. Becht proved the independence of the fluid pressure from the venous pressure although he did notice that there was normally a direct relationship between the two. (48) Fluid pressure has some relationship to the arterial pressure also, but it is still an independent identity. When the fluid pressure exceeds that of the arterial pressure, it will increase the arterial pressure. This in turn increases the fluid pressure and so the process goes on. (35)

Factors influencing the flow of the fluid from the subarachnoid space into the sinuses of the skull are numerous. The pressure of the veins is lower than that of the fluid and this tends to cause the fluid to diffuse into the blood. A rise in this venous pressure will cause a rise in the fluid pressure. (44) As some authors believe, the fluid is in osmotic equilibrium with the

blood plasma. (34) Cushing and Foley noticed that the pressure of the fluid could be lowered by the ingestion of sodium chloride. They also noticed that the pressure decreased after meals. (48) Thus we see that the osmotic tension of the blood plasma and fluid influence its absorption.

Owing to their relatively low pressure the venous blood and the fluid are driven out of the cranium with each arterial pulse, the fluid passing to the spinal subarachnoid space which is easily distensible and the blood going down into the great veins of the neck. Fluid is also pumped into and out of the ventricles by the same mechanism. This explains why substances injected into the magna may find their way into the ventricles. There are also waves trasmitted from the venous pulsations which usually occur with the phases of respiration. These are greatly exaggerated by coughing, crying, straining, etc., any forced expiration. Such actions may even double the pressure. Pressure on the neck over the juglars causes a congestion of the cerebral veins and increases the pressure of the fluid. This is the Queckenstedt phenomenon. (41)

These pulsations are responsible for the replacement of the fluid in the spinal canal whose only inflow and greatest outflow is through the cysterna magna. (51)

The interchange and replacement of the fluid in the canal is also aided by a plexus of veins in the spaces between the dura and the lamina. Engorged in forced expiration they displace the fluid in the lumbar cul-de-sac upward toward the cervical region of the cord. In spite of the pulsations there is a tendency for the cells and corpuscles to sedimentate to the lower end of the canal. (41)

BARRIER

The blood is much richer in crystalloids and colloids than the fluid, a further factor in determining the rate of flow from the subarachnoid space. Many substances may pass with ease from the cerebrospinal fluid into the blood but few can pass in the opposite direction. Tetanus antitoxin, intravenous dyes, crystalline substances by mouth, all fail to gain admittance. Although the exclusiveness of the choroid plexus is not complete, its importance therapeutically is very great. Difficult as it is for substances to pass into the fluid it is very easy for some substances to pass in the opposite direction. Crystalline substances, adrenalin, pituitary extract are all readilly absorbed (the amount that can be absorbed is remarkable). Colloids, however, are absorbed with great difficulty, probably

because of their size (molecular). (54,41,9) Stern and Gautier noticed the selctive mechanism of absorption which they called the "hematoencephalic barrier." (48) It is conceeded by most observers that under normal conditions no foreign bodies, or at least very few pass from the blood into the cerebrospinal fluid. (54) The barrier may be modified by pathology--either increase or decrease in permiability, or by metabolic changes altering the content of the various blood components in the cerebrospinal fluid. These ratios may undergo changes under normal conditions due to spontaneous fluctuations in the function of the barrier. (51)

FUNCTION

The function of the fluid has been a source of contraversy for many years. Magnedie (1825) said that the fluid "not only fills out the empty spaces in the skull and spinal anal, but has a greater function, namely, to exert a continual and regulated pressure on the neurone mass." (54) Halliburton in 1914 calls it an ideal "physiological saline solution bathing the neurones and maintaining their osmotic equilibrium." (43) He also compared it to Locke's solution which is the almost ideal fluid for nourishing and removing the waste products from tissues. (9) Cushing believes that the

fluid distributes the active principal of the pituitary gland. (54) Owing to the peculiar composition of the fluid and the selective action of the choroid plexus there is a guard against toxins and other harmful substances. The composition of the fluid suggests another function. There are small amounts of protein and sugar in the fluid. These provide the food for energy and nourishment. The wear and tear on nervous tissue is small enough to make this a possibility. Mott estimates that the carbon dioxide content is over fifty per cent. This and the fact that it recieves the products of the perivascular spaces indicates an excretory function. (9) Levinson says that the mechanical function is to maintain intracranial pressure and that other functions need further proof. (54)

COMPOSITION

The cerebrospinal fluid is a clear, colorless, saline fluid, containing small traces of protein and a few lymphocytes. According to most observers the cell count never rises over 3 per cmm. normally. Although slightly albuminous it contains no complement, fibrin ferment, haemolysin, or glycolytic ferments. It does, however, contain traces of diastase and lipase and of pituitary hormone.(41) The rate of formation and absorption is not known. It has been estimated that there is

about 120 ccm. of the fluid which is replaced from five to six times each twenty-four hours. The pressure varies according to the observer.(60-150 mm of fluid)(9)

Cotugno 1770 estimated amount at 125-156 ccm

Magendie 1825 62-372 ccm.

Mott 1910 100-150 ccm

(most observers agree with Mott)(16)

TABLE I

Ph	7.4-7.5	Levinson
Specific Gravity	1.006-1.007	Eskuchen
	1.0064-1.007	Levinson
	1.0073-1.008	Mestrezat
Freezing point	-.52 to -.58	Eskuchen
	-.56 to -.58	Levinson
	-.57 to -.59	Mestrezat
	-.56 to -.61	Depisch
Viscosity	1.01 -1.06	Eskuchen
	1.0424-1.0489	Levinson
Protein	20-30 mgm./100 ccm.	Eskuchen
	13-30	Mestrezat
Glucose	54-63	Eskuchen
	48-58	Mestrezat
Chloride	725-750	Eskuchen
	725-740	Mestrezat
Urea	6-20	Eskuchen
	3-10	Mestrezat

Phosphorus	1.5-2 mgm/100 ccm.	Cohen
	1.5-2.1	Barrio
Nitrates	.5-1	Mestrezat
Sulphur	about 1	Mestrezat
Calcium	4.6-5.7	Barrio
	5.7-6.8	Critchley & o'Flynn
Magnesium	1.4-3.5	Bario

(41)

The cerebrospinal fluid is in an osmotic equilibrium with the blood plasma and has a constancy of compositon as great as that of the blood plasma.(34)

SPINAL PUNCTURE

INDICATIONS

The indications for spinal puncture are many and varied. Spinal puncture will never become a routine examination in all cases seen by the doctor becuase of the danger and discomfort to the patient. (41) Spinal fluid is usually removed from the individual for either therapeutic or diagnostic purposes. (49)

Therapeutic spinal punctures are done for the relief of intracranial pressure, for the injection of therapeutic agents into the subarachnoid space or for the drainage or irrigations of the canals within which the fluid lies. As one author states "as a rule, a spinal puncture should be done in all cases showing signw of increase intracranial pressure with the possible exception of subtentorial tumor. (54)

Diagnostic spinal punctures are indicated when the clinical picture is such that involvement of the central nervous system is indicated. Thus it is done is cases of suspected meningits, poliomyelitis, encephalitis, hemorrhage, neurosyphilis, coma, convulsions, paralysis, etc. Do a puncture in cases where they show signs of meningeal irritation such as neck rigidity, Kernig, and retraction of the head. When meningeal signs appear following an otitis media or a infection of the air sinuses do a puncture. It is also valuable to do a lumbar puncture in cases showing subacute cerebral sympt-

oms such as headache, coma, mental confusion, loss of memory with or without focal signs, or where the patient has pain along one or more of the spinal nerves. (39) In many institutions the spinal puncture is a routine proceedure for psychopathic patients. Examination of the spinal fluid as a routine proceedure in the diagnosis of neuropsychiatrical diseases is as important as the blood studies in internal medicine. (69) Lumbar puncture is often indicated as a guide to prognosis of a disease. In syphilis spinals are done to see if the treatment has been effective and to check on the blood Wassermann. Hinton does not believe that this is necessary. He believes that if one would use a sensitive blood test, such as the Hinton test, the spinal puncture would be a proceedure of little value. (45) Chronic alcoholism is also an indication for a puncture. (50) Ives believes that if you ask yourself "Is there a prospect that spinal puncture will be an aid to diagnosis?" you will never have difficulty. (49) Malamud states that no final diagnosis of nervous and mental disease nor a differential between these and diseases of other systems is justified without a cerebrospinal fluid examination. (61)

Spinal punctures are often used in the diagnosis of tumor. Both cisternal and ventricular punctures are

used in combination with it. (4) The spinal tap is also indicated for the injection of air or other media into the subarachnoid space for the location of tumors and subarachnoid block. (54)

Lumbar punctures are also indicated in cerebral accidents. When there is a cerebral concussion with no demonsrable head injuries a puncture should be done. The mortality is nil and by the reduction of the pressure you may relieve the symptoms. Never reduce the pressure by more than one half of its original reading. In cases where there is brain laceration and contusion with brain hemorrhage you may do a puncture. You will do no good, but you also do no demonstrable harm. The mortality is almost one hundred per cent regardless of the treatment. Where there are focal symptoms after injury the eases are operative in nature and the puncture will be of no value except to relieve the post operative edema. Where they survive the first shock and later show signs of pressure at the base of the brain a puncture is of no value except as a purely diagnostic proceedure. (In these cases a low bilateral decompression may be of assisstance). (77)

CONTRAINDICATIONS

The contraindications to the spinal puncture are rather few. Hydrocephalus (internal) and tumor are most dangerous. Some authors feel that the danger in

cerebroneoplasm is overestimated. (69) When there is papilloedema puncture should not be done. (39) Erysipelas or abscesses of the lumbar region and any acute or chronic infectious entities are a contra-indication to the puncture. In general, when lumbar puncture is indicated it should not be feared because of the possible complications. (54)

PROCEEDURE

The lumbar puncture is not a highly developed technique, but it is important that the physician know the simple rules and have sufficient practice in the proceedure, if he is to obtain satisfactory results, both for his purposes and for the comfort of the patient.

The site of the withdrawal of the fluid is somewhere below the body of the second lumbar vertebrae, for this is the level at which the cord usually ends and is also the beginning of the spinal enlargement of the subarachnoid space. For practical purposes the puncture is made at about the level of the fourth interspace for this lies opposite the crests of the ilium and is therefore easily established by the superficial landmarks. Punctures may be done in the third, fourth or fifth interspace without particular danger to the patient. (41,78,89)

The puncture is done in the recumbent position Not only is the patient more stable and, in case of necessity, more easily held, but the pressure within the canal is no so great. This decrease the posibility of herneation of the brain through the foramen magnum in cases of increased intracranial pressure. It is also thought to lower the incidence of post puncture complications. The cerebros inal fluid level in the sitting position is approximately double that in the recumbent. It also enables the patient to rest while the proceedure is carried out. Lastly, the recumbent position gives a greater uniformity of results. (54)

The instruments used are more or less a matter of choice, but should have certain characteristics. The needle must be flexible and rustproof, for which reason, the needles are either of nickel or alloy and never of steel. The needle should have a rather blunt, rounded point. This not only decreases the damage done by the needle, but some abservers noted that the post puncture complications were more frequent when a sharp needle was used. (78) To decrease the damage and the discomfort of the proceedure, the needle should be of small bore--a large one is not needed except in cases where the viscosity of the fluid is greatly increased. Some authors recommend the use of special

equipment such as the Dattner needle (2) or the use of a specially fitted trocar to carry the needle through the interspinous ligament.(78) In any case the needle is to be fitted with a stylet with the one end ground even with the needle point and the other fitted into the shaft of the neddle in some way that when fully inserted the bevel of the stylet must coincide with the bevel of the needle. It is of value to have the shaft of the needle fitted so that the usual syringe may be inserted. The matter of a petcock and second exit from the needle is a matter of personal choice. (41)

The region selected for the puncture is prepared as for a minor surgical proceedure and the entire tap is done under as aseptic conditions as possible. The use of a local anesthetic is a matter of choice, but it is indicated for it not only increases the comfort of the patient, but makes the work of the investigator more likely to succeed. The patient is lain on a flat surface with the back bowed and the shoulders and hips perpendicular to the surface. The needle is forced through the ligament between the vertebrae in a line parallel to the anterioposterior diameter of the body and perpendicular to the line of the spinal column. The needle is then forced inward to the estimated depth. If an obstruction is met, the needle must be

withdrawn and another attempt made. If the needle reaches the canal there is usually a definite tearing sensation as the needle passes the dura mater of the cord. If when the stylet is withdrawn there is no fluid exuded, it is profitable to turn the needle for many times a small flap of the arachnoid may be covering the exit from the needle as though it were a one wasy valve. If, when passing the needle, the patient notices pain in an extremity it indicates that that the needle is out of line and must be corrected.

When the fluid is obtained one should first measure the pressure with a manometer, both normally and with compression of the juglars. The pulsations of the fluid should be noted. The amount of fluid is then withdrawn. One should notice the amount of the fluid which is easily removed, for Levinson believes that if more than 10 ccm. of the fluid is removed easily, a pathological condition is indicated and must be looked for with particular attention. (54)

If bloody fluid is obtained on the puncture, the needle should be withdrawn and another interspace used. If blood is still obtained the fluid may be withdrawn or another tap made at a latter ate. Bloody fluid is far from valueless. (80)

Failure to obtain fluid may be the inability to

to reach the canal as in cases with deformed vertebrae, the lack of fluid (subarachnoid block) or the thickening of the fluid so that it will no longer run through the needle. One must also be sure that it is not just an error in technique. In no instance is the withdrawal of the fluid by a syringe, except for spinal anesthesia, advisable. (54)

(41,54,9,78,39,2)

SEQUELAE

The sequelae of spinal puncture are those symptoms of central nervous system origin following the operation. There may be headache, rigidity of the neck, rise in temperature, twitching, radiating pains, inability to sit up, edema of the region and purpura (general and localized). The severity of these symptoms is proprtional to tha amount of post puncture physical change. (62) The most constant and annoying symptom is headache. Headache occurs in about 10% of the normal fluid punctures. Certain types of patients are immune to headache, however. In this groupe are the syphilities with positive serology, posttraumatic encephalopathies, and hydrocephalics. Headaches may vary in intensity and severity from a very mild headache lasting but a short time to a very excrutiating pain lasting for days. (68)

The cause of these headaches is not known. Despich and Ritcher-Quittner thought it was due to the loss of calcium. (41) The majority of the workers believe that the condition is due to the continual gradual leakage of the fluid from the sub-arachnoid space through the hole made by the needle. (2)

The treatment of the headache and other post puncture symptoms is largely a matter of prophylaxis. There are just as many headaches in hospitalized patients as in the ambulatory, but when headaches do occur, the patient in the hospital has a less severe, more transient headache. (83) Dattner showed that with the use of the Dattner needle there were only 18 headaches in 116 taps. With a ordinary needle he found that there were 6 out of 11. He believed that the Dattner needle is indicated for diagnostic punctures. (2) Wyllie gives his patients warm milk or tea after the puncture and has them lie in bed for 8-12 hours. (90) Other investigators have shown that by the injection intravenously of a.255 per cent saline solution (50 ccm.) jusst before the puncture they could decrease the incidence of headache to one in 25. (68)

When headaches do occur, the patient should remain

in bed. For the milder headaches give aspirin, caffien and phenacetin. In the very severe cases one half to 1 ccm. of pituitrin is given twice each day. (90) The use of injection of .225 per cent saline is of some help, but its effectiveness in the treatment is limited. (68)

The deaths from spinal puncture are few. They result either from the introduction of ifection (rare) or from herniation of the brain. Torbert concludes that the lumbar puncture is not too dangerous for the office, but that the physician is justified in recommending hospitalization. (83)

ROUTINE

EXAMINATION

INTRODUCTION

As we have already mentioned the earliest clinical studies of the cerebrospinal fluid were made from a therapeutic standpoint. It is not our intent to deal with this subject in this paper, however, but to describe briefly the diagnostic uses of the spinal fluid examination. The earliest work is that of Furbringer (1895) and Netter (1898) who observed cetain naked-eye changes in the fluid of meningitic and tumor patients. In 1900 Widal, Sicard and Ravout investigated the cytological characteristics of the fluid in meningitis. They later showed the importance of this examination in the diagnosis of neurosyphilis. Chemical studies of the fluid did not begin until in 1912 when Mestrezat published some exact extimations of the components of the fluid under normal and pathological conditions. Kafka applied certain biological tests to this field. Some later came the reports of reactions of the fluid with a more or less specific scope. Notable among these was the Lange colloidal gold test. This is the most valuable reaction for the estimation of the balance of the proteins in the fluid. (41)

The fluid should be examined as soon as possible after its removal from the subarachnoid space for there are certain changes which take place. In normal fluid

the first few hours will show a change in hydrogen ion concentration, a decrease in the sugar and an autolysis of the cells. In several days the color will change and and the fluid will become turbid. In pathological fluids the changes occur much more rapidly. The cells and the sugar content decrease, the Ph may rise slowly and there is a coagulant or precipitate in many cases. (54)

We shall discuss those changes observed by the naked eye or by use of simple mechanism first. It is in this order that the examinations are conducted in general practice.

PRESSURE

In every diagnostic lumbar puncture a manometer should be used. The examination is robbed of much of its value if the pressure is not noted. (39) It is true that great variations occur in the normal, but it is also true that we are able to identify definitely pathological pressures. (3) It is not saying too much to say that in come of the cases the pressure studies constitute the most important part of the fluid examination.(3)

The pressure under basic conditions remains fairly constant. There is no signifigance between the sexes or between the races. The fluid pressure of an individual

varies over long periods of time. It returns to normal in from one to three hours after the removal of from ten to fifty ccm. The fluid is replaced faster if more than twenty ccm is withdrawn. (62) The normal pressure veries from 130-150 mm. of fluid in the adult and between 45-90 mm. of fluid in the child. (41) The pressure of the fluid is of importance in many pathological conditions where it varies from the normal. The pressure is increased in syphilitic diseases, in hydrocephalics, in certain brain tumors, in the diseases of the meninges, in cerebral arteriosclerosis and disitegration, in hypertension, etc. (39,41) The pressure is also raised in congestive heart failure and is a guide to prognosis. Spinal puncture often relieves the dyspnea in these conditions. The pressure differences in the sitting and recumbent position are much more marked than in normal cases. Perhaps this explains orthopnea, where the propped up position relieves the symptoms by the decrease in the cisternal pressure. (44) Pressures below normal are unusual occuring only in tumor, subarachnoid block and general changes such as shock and fainting. Pressures below 50 occur only in those cases were there is no communication between the cranial and spinal canals. (41) The pressure is low in cases of pust puncture headache

and is often decreased in patients with long standing degenerative diseases. (3)

The pathological changes in the pressure are due to modifications of the elasticity of the dura, the intracranial arterial and venous pressure, the secretion pressure of the fluid, the rate of absorption and the amount of solid substance in the cranium. (3) Normally the pressure of the fluid is relatively independent of other factors. Weed says that the Monro-Kellie doctrine that at all times the contents of the cranium tend to remain unchanged, is true. He believes that the fact that the change in pressure on change of position is less than one would expect from the hydrostatic pressure is an indication that this is true. (87)

The amount of the pressure decrease after the removal of fluid is of importance, especially in cases of partial or complete subarachnoid block. This fact was noted by Ayala who evolved what he calls the "Quotient rachidien". This is the number of ccm. of fluid removed multiplied by the final pressure divided by the initial pressure or QxF/I. This quotient varies considerably but those under 5 indicate subarachnoid block and those over 6.5 indicates a meningeal disease. (3,41)

TURBIDITY

Turbidity is that haziness observed in the fluid which is normal clear. Turbidity may be due to a adnixture of blood, from micro-organisms, by fibrin, by cellular increase or by a combination of these. A cloudy or pussy fluid indicates meningintis, a slightly hazy fluid indicates late or early meningitis, tubercular meningitis or an anmixture of blood. (70) It is believed that as a rule it is necessary to have a cell count of300 polymorhps or 500 lymphocytes to produce turbidity. However, it is possible that the turbidity depend more on the death or.degeneration of the cellular element than on the type of cell. (41)

Turbidity is seldom a lone observation but is usually accompanied by a change in color, precipitates, coagulum,etc. Thus the appearance of turbidity is merely and indication to look for other changes in the fluid. It alone has little signifigance. (41)

FROTH

Levinson believes that all pathological fluids produce a foam on shaking. Normally there is formed only a thin froth of very short duration. He states that pathological fluids produce a film which will be thicker and last longer (at least one hour). The

thicker the foam and the greater length of time it remains the more acute is the pathology of the condition. (41)(54)

COLOR

The normal cerebrospinal fluid is always clear and colorless. Therefore, any coloration is pathological. Color may vary from a very light yellow (so light you have to look down the long axis of the container to notice) to a very deep chrome. (54)

The color of the fluid is of importance in the diagnosis of subarachnoid hemorrhage. This condition shows an evenly tinged fluid with a yellow supernatant fluid and no red cells. The first three hours after hemorrhage the fluid is yellow. in 24-48 hours it is a deep yellow and in 6-10 days becomes rather reddish. Red cells may be found in the sediment but they are usually gone by the 7-10th day. The color gradually fades until it has disappeared (3 weeks). In the puncture of a thecal vein the fluid is more intensely colored and there is always a thick coat of red cells on the tube after centrifuging.(41) When blood is present in the subarachnoid space its judicial removal, using a small calibre needle, with manometric control to prevent too rapid removal and reduction of the fluid

pressure, is a safe and beneficial proceedure. (42) Blood is present in the fluid due to trauma, infection, toxic conditions, vascular disease, neoplasm and systemic and metabolic diseases. (42)

The yellow color of the fluid has been called Xanthochromia and is of great importance in many conditions. There are many yellow fluids with little relationship to the cause or pathology. (75) The causes of xanthochromia are an increase in the protein as from transudation, a hymolytic process or an icteroid condition. They are all of signifigance in diagnosis and denote organic pathology--but not always of the central nervous system. (75) In the presence of coagulation they denote obstruction, without coagulation xanthochromic fluids suggest hemorrhage. It has been suggested that all fluids of yellow color which contain red cells be called "erythrochromic". (1)

Yellow color is of especial intrest in the presence of certain other findings. The Froin syndrome of xanthochromia, massive coagulation, increased cell count and increased protein is suggestive of subarachnoid block particularly by tumors. The absence of the massive coagulation, the incomplete Froin syndrome or the Nonne syndrome, is indicative of an incomplete block of the subarachnoid space or of a small hemorrhage.

Nonne believes that it differs from the Froin in duration and extent of the block. (1) Other observers note that the Froin appears most often in tumors of the cauds equina. They believe that the Nonn is an indication of an extramedulary tumor. (25) Diagnosis of the cause of these findings is never made from the spinal fluid examination alone. (25) In many cases the fluid above a tumor will demonstrate one of these reactions. The Froin and Nonne syndromes must be used with the Queckenstedt--the routine test for subarachnoid arachnoid patency by compression of the veins of the neck. (6)

COAGULUM

The presence of a coagulate in the fluid is often missed by the investigator because of the time required and because shaking of the fluid may prevent its appearance. This coagulum is the most delicate test fot the presence of fibrin in the fluid. The coagulate may be a very fine web or pellicle as in tubercular meningitis and syphilitic disease or a very heavy mass of material as in the Froin syndrome. Any increase in the albumin over 100 mgm. per 100 ccm. may be associated with a coagulate. There may be fibrin present without a coagulum because of the lack of fibrin ferment. For this reason many investigators add a drop of serum to

the fluid and note the result. In the case of an admixture of blood the result is hard to estimate. In such a case, if the supernatant fluid is yellow, you know there will be a coagulant. (41) The presence of a pellicle alone has no diagnostic signifiganee. (54)

VISCOSITY

The spinal fluid is only slightly more normally than that of water. An increase in this characteristic of the fluid may be associated with either an increase in the cellular or in the chemical composition of the fluid. Its presence is merely another indication for a more careful examination of the fluid--an indication which could be disregarded if the routine examinations of the fluid were satisfactory. (65)

QUECKENSTEDT

The Queckenstedt is the routine test for the patency of the subarachnoid space by compression of the veins of the neck. Its extent of and rate of rise in pressure is of importance. In every spinal puncture the Queckenstedt should be done.(3)

There are many chemical tests which may be done on the fluid obtained from lumbar puncture, but it is our intention to discuss only those which are of routine importance and mention a few of the others.

CELL COUNT

A valuable test in the routine examination of the fluid is the cell count. This is one of the most standard test that are done on the fluid. Perhaps its import nce is overestimated.

The usual cell types found in the fluid are the lymphocytes, the monocytes, the polymorhs, compound granular corpuscles, eosinophils, plasma cell, and even fibroblsts. The lymphocytes are the predominate cell type in most of the diseases except the acute coccal meningitides and abscesses. Mononuclear increase is seldom more than ten percent of the total and appears in those diseases with lymphocytosis. The polymorphs never appear in the normal fluid. They may be as high five per cent in hemorrhage, but only predominate in cases of the acute diseases already mentioned. Eosinophils appear only in the acute diseases and some of the parasitic diseases of the central nervous system. The plasma cells are never seen normally but do appear in some of the luetic diseases and diseases of degeneration. They are an indication of degeneration of the nervous tissue. The macrophages have no pathological signifigance. Fibroblasts are occasionally found in the subacute diseases and also in luetic infections. (41)

Roughly a cell count of 20-100 per cmm. is an indication of syphilis, from 300-500 of tuberculosis and from 2000-3000 of purulent meningits.(61)

The normal cell count is a subject of considerable contraversy. The earliest investigators believed that they were normally about 10 per cmm. Nonne considered that there were about 5 in a normal fluid while Levy-Valenzi, Leudde, Jeanselme and Chevalier believe that it is nearer 1½-2. For practical purposes a count of three is normal, one of 4 should be regarded with suspicion and one of 5 be considered definitely pathological. (41)(54)

Several terms will be adopted for the purpose of this paper. A count of 5-10 is slight pleocytosis, 10-50 is moderate pleocytosis, 50-250 is severe pleocytosis and 250 or more is an extreme pleocytosis.

The types of cellular increase is usually predominately lymphocytic, mixed or predominately polymorphonuclear. The lymphocytic type occurs chiefly in syphilis. It is slight in the chronic forms, in disseminated sclerosis, in herpes zoster, in poliomyelitis, in encephalitis lethargica, and in polyneuritis. The peocytosis is moderate at the inset of syphilitic disease and also occurs in the other diseases mentioned under slight pleocytosis. Severe lymphatic pleocytosis is seen but rarely in dissemminated sclerosis, herpes and encephalitis lethargica. Extreme pleocytosis with a predominance of the lymphocytes is almost never seen.

The mixed type of pleocytosis occurs usually in the cases of abscess, tumor and hemorrhage. The moderate type is seen in tuberculosis, poliomyelitis and on recovery from a cerebrospinal meningitis. The mixed type is the one most commonly seen in severe pleocytosis. It occurs in the severe and acute syphilitic diseases, in tubercular meningitis and in poliomyelitis. However, such a picture may occur in brain abscess. Extreme mixed pleocytosis is seen in the secondary stage of syphilis, in general paralysis and in tubercular meningitis.

Those types of cellular increase which are predominately polymorphonuclear (75 per cent or more) occur usually in the cerebrospinal meningeal diseases where the bacteria are found in the fluid. These types of increase are usually extreme or severe, but the moderate and slight pleocytosis may occur in abscesses and dural inflammations. (41,54,9,57,61)

The method of the examination for the cell count is a matter of personal preferance. Whether one uses the French method of centrifuging, or does a chamber count it is necessary that he thoroughly aquaint himself with the proceedure. Many of the investigators believe it is of value to do a fractional cell count. They believe that if the first fraction is lowere in cell

content than the second it proves that the process involves the brain or upper cord. This proceedure is better done by cisternal or ventricular puncture which Ayer says is safe and adequate in the right hands. (4) The type of the cell is most easily told by the smear of a centrifuged sediment of the fluid. (41)

There are many cases where the cytological findings are the same. Lucas states that all borderline cases must have a careful clinical examination--the spinal fluid findings are not enough. (57)

PROTEIN

One of the chief alterations in the spinal fluid in any pathological condition is the increase of the proteins present. Of the two types of protein in the fluid there is no known pathological condition where the globulin exceeds the albumin. There are however, conditions where the globulins approximate the albumin (general paralysis and tumors). In many cases there is a marked increase in the albumins and if the investigator does not test for the albumin as well as the globulin he may miss such diseases as acute meningitis and the arteriosclerotic diseases. (41) A quantitative protein test should be used as a routine method of fluid examination of equal importance with the pressure studies, the cell count and the Wassermann. The protein examination alone has little importance. (3)

Protein is normally present in the cerebrospinal fluid in small amounts. Any increase is patholigical. (22) The amount of the protein in the fluid is never a diagnostic feature when considered alone. Normally there is only one type of globulin present in the spinal fluid, pseudogloblin. The euglobulin and the fibrinogen appear only in the pathological conditions. They are an indication of gross pathology, but are more important for they contain the active priciple of the Wassermann reaction.(41) A protein of over 40 mgm. per 100ccm. is indicative of disease of the central nervous system. (61)

The normal protein varies from 15-45 mgm per 100 ccm. (Denis and Ayer). Other observers give a small range, Mestrezat says 15-30 while Eskuchen believes it is 20-30. (3) Malamud considers 13-30 the normal limits. (61)

Large increases in th protein content are rare but do occur. Increases of from 25-100 mgm. per 100 ccm. are common. Those from 100-500 mgm per 100 ccm. are rare but do occur. Increases of 500 or more mgm. per 100 ccm. are found only rarely in such conditions as the syndrome of Froin. (41) This syndrome consists of the approximation of the cerebrospinal fluid character to that of the blood plasma, the change taking place when

the lumbar cul-de- sac is completely cut off from the fluid in the venricles and cistera. In these cases there need not be a peivascular or perineural block. (40) May also find such a high protein content in the incomplete symdrome of Nonne. Ayer believes that the proteins transudate from the blood. Cushing is of the opinion that they arize from the tumor by a transudation process. (21) Protein increase in the blood will not tell the level of the tumor. This is done by the original concentration of the contents, the pressure studies, the Queckenstedt and the change in the character of the fluid as it flows. (21) Isolated proein increases are usually indicative of compression or tumor but may be found in arteriosclerosis and polyneuritis and localized spinal meningitis. (41) Usually the increase in the protein is accompanied by an increase in the cells. There is a rough relationship between the amount of protein and the cell count in the majority of the diseases. (41)

The protein content in a few of the pathological conditions involving the central nervous system is given below. (22)

Normal	35-100	mgm/100ccm
Ventricular fluid	less than 100	
Syphilis of the central nervous system (inactive)	50-125	

Active tabes	100-200 mgm/100ccm
Acute syphilis of the central nervous system	200-600
Lethargic encephalitis	100-200
Recent cerebral vascular disease	100-300
Tubercular meningitis	200-1000
Below compression	
Nonne	300-1700
Froin	2010 (1 case)

The presence of either euglobulin or fibrinogen is always and indication of disease. They are present in all cases where there is more than 500mgm of protein per 100 ccm. Euglobulin is found particularly in general paralysis, lues and other syphilitic diseases. Fibrinogen appears in poliomyelitis, tubercular meningitis and the acute coccal meningeal diseases. The more acute the disease the sooner the fibrinogen appears. The sensitivity of the coagulation test seems to indicate that it is the euglobulin which is missed in the majority of the cases. (41)

There are four methods used for the determination of the globulin--the Ross-Jones, the Nonne-Apelt, the Pandy, and the Noguchi. The results of the first three run parallel, but the Ross-Jones and the Pandy do not require boilong and have no odor. Of these the

Ross-Jones is the more sensitive. These are tests for the presence of the globulin but do not tell the quantity. (54)

The quantitative test for proteins is either a precipitation test similar to the Esbach urine albumen (the Nissl) or the precipitation of the protein by the use of a known standard which is read colorimetrically (Denis and Ayer). The latter is quite as accurate as any other technique described and has two main advantages. It requires a smaller amount of the fluid and less time (ten minutes or less). It also has a larger range of action. An accurate protein determination is needed in the comparison of the ventricular and cisternal fluids and in the following of a disease process. (3,22,54)

SUGAR

In 1852 Deschamps and Bussy found a substance in the fluid which would reduce the copper reagents typical for sugar reactions. Claude Bernard in 1855 demonstrated the presence of glucose in the fluid of a dog. Gorup Besanez (1862) came to the conclusion that this was not a sugar but an alcaptan. Halliburton contributed these characteristics to another compound which he called pyrocatechin. It was in 1897 that Nawratzki found that this copper reducing substance formed

crystals of glycozone, was reduced by Fehling's, was fermented by yeast and rotated the plane of polarized light the same as glucose. Deniges working independently published results of a quantitative estimation of this reducing substance and also proved that its power of rotating the plane of polarized light was similar to that of glucose (in 1898). Recent investigators have shown that not all of the reducing substance is glucose. Folin and Berglund estimated that at times the non-glucose portion exceeded more than ten per cent of the total reducing substance. Although this complicates the study of the fluid sugar, if the ratio of the fluid sugar to the blood sugar is used, the results would not differ greatly (the blood also contains some non-glucose reducing substances. (81,32) This consideration would not interfere nor decrease the value of the sugar level in differential diagnosis.

The amount of sugar in the fluid of an individual is not constant. It is more or less dependent of the blood sugar level although there is no direct relationship between the two. (32) The ingestion of carbohydrates increase the sugar content of the fluid. The fluid sugar is also raised in diabetes. The blood sugar exceed the fluid sugar in all normal and

and pathological conditions. (13) Normal fluid contains about 55 (14) to 70 (13) per cent of the blood sugar. The normal sugar content of the fluid is from 48-58 mgm. per 100 ccm. (41)

An increase in the sugar level of the fluid is usually due to the rise of the blood sugar. This is true in diabetes and other general systemic diseases such as small pox, pertussis and mumps. There may be a slight increase in cases of increased intracranial pressure possibly due to the increased permiability of the barrier. (41) It was once thought that an increase in the sugar level of any magnitude was pathognomonic of encephalitis lethargica. This has been disproven. (15)

Roughly, a decrease in the sugar content is confined to infectious meningitis. (90) An absence of hypoglycemia with a fluid sugar of less than 50 mgm. per 100 ccm. is indicative of an acute infection of the meninges. (32) In cases of meningitis there may be a total loss of the glucose or the small amount remaining may disappear on standing due to the glycolytic ferments in the cells or the utilization of the glucose by the organisms. (41) A decrease in the sugar is the only positive finding, for the sugar may be normal or slightly lower than normal and still have a meningitis. (73)

There may be a decrease in the sugar in untreated cases of syphilis which returns to normal on treatment. (79) The return of the sugar toward the normal in cases of meningitis is a good indication that the patient is improving. (74) In some instances the protein may mask the presence of the sugar in the fluid and lead to a false impression that the sugar is decreased. (41) The change of the sugar level in the cerebrospinal fluid is little help in diagnosis when considered alone and only a decrease is of any importance when it is used in conection with the other tests.

CHLORIDES

The content of the fluid chlorides varies directly with that of the blood plasm, but the quantitative distribution between them is influenced by the protein content of the blood and the fluid. The chloride content is always higher than that of the blood--possibly because of the lack of colloids in the fluid to maintain the osmotic pressure. (32) The content of the ventricular, cisternal and lumbar fluids is the same.(41)

The normal chloride content of the fluid is 720-760 mgm. per 100 ccm. Any variation above or below this range is thought to be pathological. (41) The chlorides

are increased in the cardiovascular and renal diseases. (61) A decrease in the chlorides usually occurs when there is an increase in the protein content of the fluid. However, this would account for only a portion of the chlorid decrease. One must evaluate the chloride content in relation to that of the blood. Children often have a decrease in chlorides and even a meningismus following a persitent vomiting attack. (39) A decrease in the chlorides is the rule in the meningitides. Here there is a gradual decrease in the content as the disease process develops. It may go as low as 650-680 mgm. per 100 ccm. in coccal meningitis, but reaches levels of 500-600 mgm. per loo ccm. only in tubercular meningitis. The chlorides may be decreased in pneumonia and are decreased in typhus and typhoid fever. In the latter,however, the drop is early and complete--not the gradual decrease seen in infectious meningitis. (41) The chloride is of particular value when considered in conjunction with the sugar content of the fluid. A decrease in both sugar and chloride is indicative of an infectious meningitis. Chlorides are also important in the prognosis of a condition. The lower the chloride the graver the prognosis and vice versa. (32)

The chlorides may be estimated by the van Slyke

or the Seelman method. (32, 54) The Seelman is perhaps a little superior for although it is not quite as accurate as the other, it requires less fluid.

IMMUNOLOGICAL TESTS

WASSERMANN REACTION

Since the usual antibodies of the blood are not present in the blood the number of tests for these immune bodies is of no value. The antibodies which do occur in the fluid are produced by the action of the organism on the nervous tissue and meninges. In cases of meningococcus meningits it is valuable to test for the antibodies. If a meningitis is of the meningeal type the smear, culture and the immunological reactions will be sufficient differential diagnosis.

The only routine examination of the immunological type done on the spinal fluid is the Wassermann. This is a specific test for syphilitic involvement. To get the most from this reaction it should be used in connection with a coloidal reaction--another routine proceedure. The Wassermann active substance and the colloidal reactant are different factors in the spinal fluid. The Wassermann substance is contained in the globulin portion. The filterability of this globulin is decreased in syphilis. (66) Most authors consider

a positive reaction to be specific for syphilis, but they do not believe that a negative reaction rules out the disease. (54) The Kahn reaction is also used for the diagnosis of syphilis of the central nervous system, but the Wassermann reaction gives higher percentage of positive reactions in treated and untreated cases of paresis than does either the standard or modified Kahn. The standard Kahn is less sensitive than the modified Kahn. (72) Although the Kahn technique is quicker and simpler than the Wassermann, the standard Kahn is not sensitive enough, nor the modified Kahn accurate enough to replace the Wassermann.(54)

Active syphilitics disease of the nervous system has been found although the spinal fluid was negative. Negative bloods are common with a positive fluid. In 50 percent of the Wassermann fast cases of one authors series had a positive fluid. In the same series we find that 67.6 per cent of the patients whose blood relapsed had a positive fluid Wassermann. Of the latent syphlitics, 30 per cent had a positive fluid reaction on entry. Thus we see that the blood Wassermann can not replace the fluid Wassermann. (37) Although the diagnosis of syphilis of the central nervous system may be made from the Wassermann reaction, the type of involvement must be determined by clinical

picture and other spinal fluid findings.

COLLOIDAL REACTIONS

The technique of the colloidal gold test was first described by Lange in 1912. Lange got hid ideas from Zsigmondy who called attention to the precipitation of colloidal gold chloride by electrolytes and their protection by proteins. He used the gold number in his experiments. This was the amount of protein which would protect 10 ccm. of the colloidal gold from preciptiation by 1 ccm. of 10 per cent sodium chloride. He used his number in some experimental work. (18) In 1914 Miller and Levy found that the reaction in the paretic and luetic fluid differed. Hames in 1917 claimed that the test was very sensitive. You might get a gold curve without a positive Wassermann, but you would not get a positive Wassermann that did not effect the gold sol. Weston in 1918 proved that the gold precipitant was not the Wassermann reactive substance. (63) Cruickshank in 1920 consisered that the zone of the reaction depended on the ratio of the relative amounts of albumin and globulin. (18)

The Lange colloidal reaction is one of three such types. There is also the colloidal benzoin and mastic reactions. These are all physiochemical methods for the determination of the ablumin globulin ratio of

the cerebrospinal fluid. When these two are compared with the colloidal gol test they are proven of about equal value. Cockrill concludes that since the benzoin is the simplest and its reagents are the most stable this is the method of choice in routine examination of the fluid. (11) This does not hold if the fluid is such that the entire original test of 16 tubes had to be used. Levinson believes that the Lange is the most valuable because that its reactions are sharp and easily read. He believes that the other test should be used only for collaboration of the Lange.(54) Some authors have suggested modifications of the Lange test. Boerner noticed that varying amounts of fluid could be used if the proportions were kept the same. (8) Mellanby and Anwyl-Davies method of colloidal gold is more sensitive, more reliable, and more easily done. (63) It is more efficient than the original Lange. (38)

The gold sol is precipitated by paretic, sometimes by luetic, but never by normal fluid. The gold sol can be sensitized by the addition of acid or desensitized by base. Addition of acid will give a paretic curve in normal fluid. The precipitation of the gold by ammonium sulphate is due to the removal of the normal alkalinity and not to a change in the normal albumin

globulin ratio. (76)

The colloidal gold reaction is due to the presence of a precipitationg substance in the fluid. There are both precipitating and protecting substances in the pathological fluids. Albumin and globulin may both have the power to react as percipitants and protectors of the colloidal solution. (66) Some believe that the pseudoglobulin has a negative charge while the euglobulin has a positive charge and that it is the balance between these two which decides the reaction. (63) The pricipitating substance is not dialysable, is precipitated by one half saturation with ammonium sulphate or by 50 per cent alcohol at 0 degrees Centigrade, and is destroyed by heat. (63) The change in the state of the protein modifies its powers. The salt solution that is added in the proceedure tends to partially neutralize the action of the protector. (66)

The test is read by the change in the colloidal gold in each of a series of ten tubes. As the state of the gold sol changes the color also changes. The extent of the color change is read as 1,2,3,4,5, or 0. The readings are recorded in the series the tube with the greatest concentration of the fluid coming first. (41) Reactions in the first and third zones are quite specific for general paralysis and non-luetic meningitis, resp-

ectively. Those reactions in the middle zone give curves which are less uniform (a tabes) but do always seem to indicate central nervous system lues. (38)

Although the gold sol test is of value in the diagnosis of central nervous system syphilis, they are of equal importance after a few weeks of antiluetic treatment. (39)

BACTERIOLOGICAL EXAMINATION

A bacteriological examination should be made in all cases with meningeal syndromes. (61) These consist of a direct smear of the fluid and culture of the organisms, if any. Several types of media are innoculated. There are very few organisms that will not grow on agar, blood agar, ascitic dextrose agar, brain broth or glucose agar. (54) Organisms may be found in patients without any meningeal signs, but evidently their presence had not initiated any pathological response. (71)

MISCELLANEOUS

Calcium in the fluid is normally about 6.2 mgm. per 100 cdm. This level remains rather constant and there is no relationship between the calcium level and the pressure, cell count, protein and the Lange and Wassermann reactions. It is decreased in tetany (returns to normal before the blood calcium) and

increased in the syndrome of Froin. Calcium is not an aid to diagnosis. (17)

Normal phophorus content of the fluid is 1.25 to 2 mgm. per 100 ccm. In meningitis there is and increase in this element. It is slightly higher in the chronic infectious diseases. The increase in the phosporus content in life is due to the change in the permiability of the barrier. After death there is an increase due to the lipoidal breakdown. Phosphorus content of the blood is independent of the blood content, age, proximity of death, cell count or protein content of the fluid, previous puncture or bacterial activity. (12)

The bromide quotient is a test for the permiability of the barrier. It is used chiefly in cases where the therapeutic agents must function by way of the blood vessel changes. A high quotient indicates an increase in the permiability of the barrier.

The permanganate reduction index is that amount of decinormal permanganate which, boiled for 10 minutes in strong acid, is reduced by 1 ccm. of spinal fluid. The index is increased in pathological conditions. An index below 2 is normal, 2-2.5 are borderline indeces and above 2.5 the index is indicative of pathology. (46)

The only consistent ferment change in the spinal fluid is that of catalase. There is none in the normal

fluid but it is present in such diseases as meningitis. While the presence of the catalase indicates a high cell count or a coaculum, it yields no information which can not be told immediatley from the cell count (56)

BLOODY FLUID

The presence of blood in the fluid does not rob it of all diagnostic value. The cell count may be estimated by subtracting one white cell for each 500 red cells. If there are less than 300 red cells per cmm. the globulin test is signifigant. The original protein of the fluid would equal the protein of the bloody fluid minus .0008 times the red count of the fluid. You can generally diregard the contamination in so far as sugar is concerned for it would take enough blood to make the red cell count of the fluid 100,000 per cmm. in order to raise the sugar 3 mgm. To lower the chlorides 3o mgm. per 100 ccm. it would require a 20 per cent admixture of blood. The reaction of the fluid on gold sol is not valueless although a contamination of 25,000 red cells per cmm. will cause a rise in the middle of the curve. The mastic reaction is less sensitive to contamination by the blood. The Wassermann reaction, if negative, is as reliable as that on uncontaminated fluid. If positive it may mean that there is a positive blood, not fluid test. (80)

SUMMARY

A routine examination of the spinal fluid should contain at least the pressure studies, the the physical properties of the fluid, the globulin test, the total protein, the Wassermann, the colloidal gold and the bacteriological examination (if indicated). The sugar and the chloride are of value, particularly in the diagnosis of the infectious meningitides, and should be determined. Other tests are of value chiefly to confirm those done routinally and for further specific study. (61,65)

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